UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/531,099	04/07/2005	Yukimasa Shiotsu	09859/0202758-US0	2120

7278 7590 03/30/2009

DARBY & DARBY P.C.
P.O. BOX 770
Church Street Station
New York, NY 10008-0770

EXAMINER	
BROOKS, KRISTIE LATRICE	
ART UNIT	PAPER NUMBER
1616	
MAIL DATE	DELIVERY MODE
03/30/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/531,099	SHIOTSU ET AL.	
	Examiner	Art Unit	
	KRISTIE L. BROOKS	1616	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *07 April 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-5,7-11,25-29,35 and 41* is/are pending in the application.

4a) Of the above claim(s) *1,3-5,7,9-11,25,27-29,31 and 33-35* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *2,8,26 and 32* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *1-5,7-11,25-29,35 and 41* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *07 April 2005* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *6/28/05*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

1. Restriction is required under 35 U.S.C. 121 and 372.

This application contains the following inventions or groups of inventions which are not so linked as to form a single general inventive concept under PCT Rule 13.1.

In accordance with 37 CFR 1.499, applicant is required, in reply to this action, to elect a single invention to which the claims must be restricted.

Group I, claim(s) 1,3,5,7,9,11,25,27,29,31,33, and 35, drawn to a therapeutic agent or composition comprising a steroid-sulfatase inhibitor and an agent for hormone therapy and/or an agent for chemotherapy.

Group II, claim(s) 2,8,26 and 32, drawn to a method for treating hormone dependent cancer comprising administering a a steroid-sulfatase inhibitor and an agent for hormone therapy and/or an agent for chemotherapy.

Group III, claim(s) 4,10,28, and 34, drawn to a kit comprising a steroid-sulfatase inhibitor and an agent for hormone therapy and/or an agent for chemotherapy.

2. The inventions listed as Groups I-III do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons:

The technical feature linking the species is the combination of the steroid-sulfatase inhibitor and agent for hormone therapy and/or an agent for chemotherapy. However, Li et al. (US 6,288,050) teach steroid-sulfatase inhibitors in combination with an agent for hormone therapy and/or an agent for chemotherapy. Therefore, there is lack of unity a posteriori because the technical feature linking the species does not define a contribution over the prior art.

3. This application contains claims directed to more than one species of the generic invention. These species are deemed to lack unity of invention because they are not so linked as to form a single general inventive concept under PCT Rule 13.1.

The species are as follows:

A sulfatase inhibitor corresponding to formula I, IA, and IB.

Applicant is required, in reply to this action, to elect **one** formula selected from formula I, IA, or IB, a single species of the elected formula, to which the claims shall be restricted if no generic claim is finally held to be allowable. **The reply must also identify the claims readable on the elected species, including any claims subsequently added.** An argument that a claim is allowable or that all claims are generic is considered non-responsive unless accompanied by an election.

Upon the allowance of a generic claim, applicant will be entitled to consideration of claims to additional species which are written in dependent form or otherwise include all the limitations of an allowed generic claim as provided by 37 CFR 1.141. If claims are added after the election, applicant must indicate which are readable upon the elected species. MPEP § 809.02(a).

4. The claims are deemed to correspond to the species listed above in the following manner:

They all comprise a sulfatase inhibitor.

The following claim(s) are generic: 1

The species listed above do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, the species lack the same or corresponding special technical features for the following reasons:

The technical feature linking the species is the combination of the steroid-sulfatase inhibitor and agent for hormone therapy and/or an agent for chemotherapy. However, Li et al. (US 6,288,050) teach steroid-sulfatase inhibitors in combination with an agent for hormone therapy and/or an agent for chemotherapy. Therefore, there is lack of unity a posteriori because the technical feature linking the species does not define a contribution over the prior art.

Notice of Possible Rejoinder

5. The examiner has required restriction between product and process claims. Where applicant elects claims directed to the product, and the product claims are subsequently found allowable, withdrawn process claims that depend from or otherwise require all the limitations of the allowable product claim will be considered for rejoinder. All claims directed to a nonelected process invention must require all the limitations of an allowable product claim for that process invention to be rejoined.

In the event of rejoinder, the requirement for restriction between the product claims and the rejoined process claims will be withdrawn, and the rejoined process claims will be fully examined for patentability in accordance with 37 CFR 1.104. Thus, to be allowable, the rejoined claims must meet all criteria for patentability including the requirements of 35 U.S.C. 101, 102, 103 and 112. Until all claims to the elected product are found allowable, an otherwise proper restriction requirement between product

claims and process claims may be maintained. Withdrawn process claims that are not commensurate in scope with an allowable product claim will not be rejoined. See MPEP § 821.04(b). Additionally, in order to retain the right to rejoinder in accordance with the above policy, applicant is advised that the process claims should be amended during prosecution to require the limitations of the product claims. **Failure to do so may result in a loss of the right to rejoinder**. Further, note that the prohibition against double patenting rejections of 35 U.S.C. 121 does not apply where the restriction requirement is withdrawn by the examiner before the patent issues. See MPEP § 804.01.

Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

Telephone Election

During a telephone conversation with Attorney Louis Deljuidice on March 19, 2009 a provisional election was made with traverse to prosecute Invention II and formula IB, as the election of species, claims 2,8,26, and 32. Affirmation of this election must be made by applicant in replying to this Office action. Claims 1,3-5,7,9-11,25,27-29,31, and 33-35 withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention.

Applicant is advised that the reply to this requirement to be complete must include (i) an election of a species or invention to be examined even though the

requirement may be traversed (37 CFR 1.143) and (ii) identification of the claims encompassing the elected invention.

The election of an invention or species may be made with or without traverse. To preserve a right to petition, the election must be made with traverse. If the reply does not distinctly and specifically point out supposed errors in the restriction requirement, the election shall be treated as an election without traverse.

Status of Application

6. Claims 1-5,7-11,25-29, and 31-35 are pending. Claims 1,3-5,7,9-11,25,27-29,31, and 33-35 are withdrawn from further consideration as being drawn to the nonelected invention.

Claim Rejections - 35 USC § 112, 1st

7. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

8. **Claims 2,8,26 and 32 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for treating hormone-dependent cancers associated with breast cancer, does not reasonably provide enablement for treating <u>all</u> hormone-dependent cancers. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.**

The factors to be considered in determining whether a disclosure meets the enablement requirement of 35 U.S.C. 112, first paragraph, have been described in *In re Wands*, 8 USPQ2d 1400 (Fed. Cir. 1988). Among these factors are: 1) scope or breadth of the claims; 2) nature of the invention; 3) relative level of skill possessed by one of ordinary skill in the art; 4) state of, or the amount of knowledge in, the prior art; 5) level or degree of predictability, or a lack thereof, in the art; 6) amount of guidance or direction provided by the inventor; 7) presence or absence of working examples; and 8) quantity of experimentation required to make and use the claimed invention based upon the content of the supporting disclosure. When the above factors are weighed, it is the Examiner's position that one skilled in the art could not practice the invention without undue experimentation.

Scope or breadth of the claims

The scope of the claims is drawn to treating any hormone-dependent cancer by administering a steroid sulfatase inhibitor and an agent for hormone therapy and/or chemotherapy. Hence, the claims are very broad.

Nature of the invention

The nature of the invention is directed to a method for treating any hormone-dependent cancer by administering a steroid sulfatase inhibitor and an agent for hormone therapy and/or chemotherapy.

State of, or the amount of knowledge in, the prior art

The art teaches that the enzyme steroid sulfatase (STS) regulates the local production of estrogens and androgens. STS inhibitors are expected to block the local production and consequently reduce the local levels of the hormones. They have been considered potential new therapeutic agents for the treatment of estrogen and androgen dependently disorders. In the treatment of hormone-dependent cancer, most studies on STS inhibitors are aimed at providing novel therapeutics for the treatment of breast cancer (see the abstract and pages 533-534 of Nussbaumer et al. Steroid Sulfatase Inhibitors, *Medical Research Reviews*, Vol. 24, No. 4, 529-576, 2004).

Thyroid cancer is the most common endocrine cancer but is still a relatively rare disease. The thyroid gland produces thyroid hormones (TSH) that regulate metabolism, growth, and development. Treatment options for thyroid cancer include surgery, radioactive iodine treatment, thyroid hormone therapy and chemotherapy. (see Scott, Thyroid cancer in adults, Radiologic Technology, Jan/Feb 2009, Vol. 80/No.3, pages 241-242, and 254-261).

The art teaches that the main treatment of prostate cancer is hormonal therapy with steroidal antiandrogens, estrogens, nonsteroidal antiandrogens, LHRH agonists, and that the treatment of patients with high-grade tumors in prostate cancer still remains largely incurable with significant morbidity (Abstract, EI- Rayes et al., Hormonal therapy

for prostate cancer: past, present and future, Experimental Review in.Anticancer Therapy, 2(1), 37-47 (2002)).

Level or degree of predictability, or a lack thereof, in the art

Applicant broadly claims "A method for treating a hormone-dependent cancer", by administering a steroid sulfatase inhibitor and an agent for hormone therapy and/or chemotherapy.

It is known in the art that steroid sulfatase inhibitors are useful in treating some hormone dependent cancers, such as, breast cancer. However, current treatment options centering on thyroid cancer include thyroid hormone therapy, chemotherapy, surgery, etc. There is no current treatment of drawn to treating thyroid cancer with steroid sulfatase inhibitors. Furthermore, treatment of patients with high-grade tumors in prostate cancer still remains largely incurable with significant morbidity. Therefore, it cannot be established that the steroid sulfatase inhibitors are capable of treating any hormone dependent cancer. The specification provides evidence that the instant compounds are capable of reducing proliferation in breast cancer cells. However, there is no guidance or data to support that the instant compounds will function to treat all hormone-dependent cancers. Thus, there is a high level of unpredictability as to whether the instant compounds will function to treat all hormone-dependent cancers.

Amount of guidance or direction provided by the inventor

The specification does not provide any guidance as to how to treat all types of hormone-dependent cancers.

Presence or absence of working examples

The specification provides 2 Examples. Both of which are drawn to the proliferation inhibition of breast cancer cells using the combination of an antiestrogen agent or aromatase inhibitor and a steroid sulfatase inhibitor. The combination reduced cell proliferation in breast cancer cells. However, there are no examples drawn to treating any other type of hormone-dependent cancer.

Quantity of experimentation required to make and use the claimed invention based upon the content of the supporting disclosure

One of ordinary skill in the art would have to conduct a myriad of experimentation to determine if the instant steroid sulfatase inhibitors are effective at treating all hormone-dependent cancers. There is no one compound known to treat all types of hormone-dependent cancers, as each cancer involves different receptors, mechanisms of action, etc., thus requiring a specific regimen as to how each cancer will have to be treated. As a result, one of ordinary skill in the art would be required to conduct an undue amount of experimentation.

For the foregoing reasons, Applicant is not enabled for treating all types of hormone-dependent cancers.

Claim Rejections - 35 USC § 103

9. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

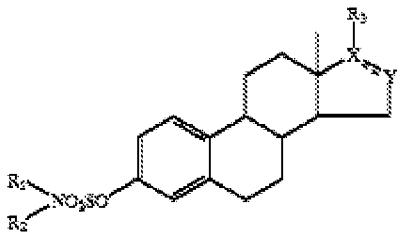
10. Claims 2, 8, 26, and 32 are rejected under 35 U.S.C. 103(a) as being unpatentable over Li et al. (US 6,288,050) in view of Labrie et al. (US 5,393,785).

Applicant claims a method for treating a hormone-dependent cancer, which comprises administering a) a steroid-sulfatase inhibitor and b) an agent for hormone and/or an agent for chemotherapy together or separately at an interval.

Determination of the scope and content of the prior art

(MPEP 2141.01)

Li et al. teach steroid sulfatase inhibitors of formula II,



wherein R_1 an R_2 are hydrogen,R_3 is selected from , and R_7 is a straight chain alkyl having 1-14 carbons (see the abstract, column 3 lines 50-67, and column 4 lines 1-26). The estrone sulfatase inhibitors of the invention are provided with anti-tumor or synergistic activity and can be combined with anti-estrogen and aromatic inhibitors (see column 3 lines 9-11). Li et al. teach a method of the treatment of estrogen dependent illnesses, such as, breast cancer, vaginal cancer, endometrial cancer, ovarian cancer, and endometriosis (see column 8 lines 64-67 and column 9 lines 1-2). The method includes incorporating one or more compounds of formula II in a pharmaceutically acceptable carrier and administering a therapeutically acceptable dosage to a patient (see column 9 lines 3-8).

Ascertainment of the difference between the prior art and the claims (MPEP 2141.02)

Li et al. teach the instant steroid sulfatase inhibitors can be combined with antiestrogen compounds but do not teach any antiestrogen compounds or exemplify the

combined administration of a steroid sulfatase inhibitor and an antiestrogen. This deficiency is cured by the teaching of Labrie et al.

Labrie et al. teach antiestrogenic compounds of formula I for the treatment of estrogen dependent diseases (see the abstract and column 2 lines 30-48). The diseases include breast cancer, ovarian cancer, endometriosis, etc. (see column 2 lines 22-27).

Finding of prima facie obviousness

Rational and Motivation (MPEP 2142-2143)

One of ordinary skill in the art would have been motivated to administer steroid sulfatase inhibitors in combination with antiestrogenic compounds because Li et al. suggests the combination in the treatment of estrogen dependent illnesses. Furthermore, it is know in the art that antiestrogenic compounds are useful for treating estrogen dependent illness, such as, breast cancer, ovarian cancer, endometriosis, etc., as suggested by Labrie et al.

Thus, it would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to administer a steroid sulfatase inhibitors in combination with antiestrogenic compounds to a patient in need because of the added therapeutic benefit in the treatment of estrogen dependent illness.

Therefore, the invention as a whole would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the reference, especially in the absence of evidence to the contrary.

Conclusion

11. No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to KRISTIE L. BROOKS whose telephone number is (571)272-9072. The examiner can normally be reached on M-F 8:30am-6:00pm Est..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Johann R. Richter can be reached on (571) 272-0646. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

KB

/Johann R. Richter/
Supervisory Patent Examiner, Art Unit 1616